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Are Substances Found In Green Tea Effective In Reducing Inflammatory And Noninflammatory Lesion Counts In Men And Women With Acne Vulgaris?

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Are Substances Found In Green Tea Effective In Reducing Inflammatory And Noninflammatory Lesion Counts In Men And Women With Acne Vulgaris?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

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Abstract

OBJECTIVE: The objective of this selective EBM review is to determine whether or not the substances found in green tea are effective in reducing noninflammatory and inflammatory lesion counts in men and women with acne vulgaris.

STUDY DESIGN: Systemic review of two double-blind RCTs and one case study published after 2008, all in the English language.

DATA SOURCES: Data sources obtained for this review were found using PubMed, published in peer-reviewed journals and selected based on relevance to the clinical question, outcomes measured and date published.

OUTCOMES MEASURED: The outcomes were measured based off of reduction in total lesion counts, patient satisfaction (defined as full satisfaction, partial satisfaction or no satisfaction), and a Leeds score which is a common, objective technique used by dermatologists to assess inflammatory and noninflammatory acne lesions.

RESULTS: All three studies showed significance in decreasing total lesion counts with the use of green tea products. Yoon et al. showed statistical significance between each epigallocatechin-3-gallate (EGCG) treated group and baseline, and statistical significance between each EGCG-treated group and control. In Lu et al. green tea extract significantly reduced lesion counts on the nose, perioral area and the chin with a $P<0.05$. Additionally, in Elsaie et al. the decrease in total lesion counts was also statistically significant with a $P<0.0001$ after use of a topical green tea lotion.

CONCLUSIONS: The use of the anti-inflammatory polyphenol epigallocatechin-3-gallate in green tea could be a potential low-cost, natural alternative medicine for the treatment of acne.

KEY WORDS: acne vulgaris, green tea, epigallocatechin-3-gallate (EGCG)

INTRODUCTION

Acne vulgaris is defined as a chronic inflammatory disease of the pilosebaceous units characterized by erythematous papules, pustules and comedones, and which can eventually lead to scarring.[1] It is the most common skin disorder affecting adolescents and young adults with a prevalence ranging from 35% to over 90% and it can persist past the third decade.[2] In 2013 it was estimated that 5.1 million Americans sought treatment for acne vulgaris and $400 million were lost in productivity for patients and caregivers.[3] On top of the financial burden this condition holds upon the country, acne has shown to cause significant psychological and social effects of embarrassment, anxiety and insecurity, as well as physical effects in terms of life-long scarring and disfiguration.[4] Therefore, it is of utmost importance that clinicians are well versed in finding the most effective treatments for each individual patient for the sake of the person suffering as well as for the financial burden the condition takes on the country.

The four main factors involved in the pathophysiology of acne are: follicular hyperkeratinization, increased sebum production, *Propionbacterium acnes* within the follicle, and inflammation.[2] During the prepubertal period, there is a significant increase in sebum as the sebaceous glands enlarge; this sebum creates a medium of growth for *P. acnes* causing the bacteria to thrive.[2] There are also multiple external factors which play a role in the development and persistence of acne such as family history, diet, stress, insulin resistance and BMI. Studies have shown that 85% of adolescents in the US are affected by acne.[4] Though much progress has been made throughout the past decade in terms of discovering the physiological process behind acne, the interactions between them are complex. Additionally, many of the treatments available only have modest efficacy and do not always target all four factors of acne development.

First line medications for acne treatment typically include topical medications such as retinoids, benzyl peroxide, and salicylic acid.[5] These medications are best for mild acne and take four to eight weeks to see improvement but have been shown to cause burning and irritation.[4,5] Antibiotics such as tetracyclines can be prescribed to reduce inflammation and as a bacterostatic, which stops bacteria from reproducing, but this treatment poses a risk for antibiotic resistance and gastrointestinal side effects.[5] Isotretinoin and hormonal therapies are the only treatments that decrease sebum production.[4] Although effective, isotretinoin comes with the risk of teratogenicity, dyslipidemia and liver damage, and needs to be highly monitored throughout its course.[4] Hormonal therapy, such as birth control pills, is a good option in some young women but not an option in males.

It is clear that there is still more research to be done in finding more effective, less costly treatments with minimal side effects for acne vulgaris. With a rapid increase in complementary, alternative medicine in Western countries, the major polyphenol epigallocatechin-3-gallate (EGCG) found in green tea has received increased attention. Epigallocatechin-3-gallate has been shown to have potent antimicrobial, anticarcogenic, and anti-inflammatory properties as well as the ability to modulate the production and actions of androgens and other hormones.[1,4] Therefore, green tea, a cost-effective, more generally safe, natural substance could potentially play a role in decreasing and treating acne vulgaris. This systematic review evaluates two double blind RCTs (randomized controlled trials) and one case study to determine if the EGCG in green tea can effectively reduce lesion counts in men and women with acne vulgaris.

OBJECTIVE

The objective of this selective EBM review is to determine if the substances found in green tea are effective in reducing inflammatory and noninflammatory lesion counts in men and women with acne vulgaris.

METHODS

Two double-blind, randomized control trials and one case study were selected for this systemic review. Criteria for their selection included their relevance to the clinical question, population studied and outcomes measured in patient-oriented results. Each study chosen evaluated the efficacy of green tea and its polyphenol EGCG in reducing lesion counts of men and women aged 15-45 with acne vulgaris. The subjects in Ji et al. were treated with 1% or 5% EGCG solution on one half of their face twice per day for eight weeks, while the subjects in Lu et al. had a daily dose of oral EGCG for four weeks.[4,6] Lastly in Elsaie et al. 2% green tea lotion with ethanol was applied on lesions twice daily for six weeks.[1] Effectiveness was determined through total lesion counts in all trials and also through patient satisfaction.

"Acne vulgaris", "green tea" and "epigallocatechin-3-gallate" were the keywords used to search for double-blinded RCTs published in peer-reviewed journals via PubMed. All studies were published in English within the past 10 years, after 2008. Cochrane systemic reviews were excluded as well as studies in which the patients did not have a clinical diagnosis of acne vulgaris. If the study's results were not applicable to patient outcomes, they were additionally exempt from the systemic review. In the Lu et al. study, women who had systemic retinoid or hormone treatment in the past three months and/or women who had a systemic disease or dermatologic condition that could skew results were excluded from the study.[6] Table 1 demonstrates the demographics and characteristics of the selected reviewed studies. Statistics

used to evaluate efficacy of the treatment included the p value and numbers needed to harm, NNH.

Table 1: Demographics and characteristics of included studies

Study	Type	# of Pts	Age (Yrs)	Inclusion Criteria	Exclusion criteria	W/D	Interventions
Elsaie, 2009[1]	Case Study	20	15-36	Men and women with mild to moderate acne vulgaris who were outpatients in a Dermatology National Research Centre clinic	Not listed in article	0	2% green tea lotion (100ml) with ethanol (25ml) applied x2 daily for 6 weeks
Ji, 2013[4]	Double blind, split faced RCT	37	Mean age 22.1	Men and women with mild to severe facial acne vulgaris	Not listed in article	2	1% or 5% EGCG solution (the major polyphenol in green tea) on one side of face (chosen randomly) x2 per day for 8 weeks

Table 1: Demographics and characteristics of included studies

Study	Type	# of Pts	Age (Yrs)	Inclusion Criteria	Exclusion criteria	W/D	Interventions
Lu, 2016[6]	Double blind RCT	80	25-45	Women aged 25-45 years old with moderate-severe acne vulgaris	Women who had systemic retinoid or hormone treatment in the past 3 months and/or women who had a systemic disease or dermatologic condition that could skew results	16	1 decaffeinated green tea extract capsule 30 minutes after a meal daily for 4 weeks

OUTCOMES MEASURED

The common outcome measured in all three studies was the total lesion counts on the patients. In Elsaie et al. a total lesion count (TLC) of all patients in the trial was taken by adding together the papules and pustules on the patients' faces. A severity index (SI) was also created through the total lesion counts, <10 lesion was given an SI of 1, 10-20 lesions was given an SI of 2, and >20 lesions was given an SI of 3. These outcomes were measured every two weeks after the start to the end of the trial at six weeks.

In Ji et al. a revised Leeds score was used to calculate total number of lesions. The Leeds score takes into account inflammatory lesions, such as papules, nodules, pustules and cysts, as well as noninflammatory lesions, such as comedones. Ji et al. also used a visual analogue score (VAS) to analyze patients' subjective assessments of their acne. At the beginning of the study each patient's VAS was a 10 and they subjectively judged the severity of their acne and whether

it was improving or worsening through the eight weeks. Leeds score and VAS were taken every two weeks of the eight-week trial.[4]

Lastly, in Lu et al. total lesion counts (including inflammatory and noninflammatory lesions) were recorded on each patient in the trial by dermatologists who did not know which patients were in the experimental group or control at baseline and after four weeks.[6]

RESULTS

For this systemic review two randomized double-blind trials and one clinical trial were selected to determine the efficacy of substances from green tea in decreasing lesions counts in patients with acne vulgaris. All three studies used data based off of an intention-to-treat analysis. The analysis of outcomes is based off of improvement in inflammatory and noninflammatory lesions from acne vulgaris.

In Elsaie et al. 20 patients (6 males, 14 females) were enrolled in the study between the ages of 15-36 with mild to moderate acne vulgaris. They were all currently outpatients at the same dermatology clinic. Patients enrolled were instructed to apply 2% green tea lotion which was crafted with 100ml of brewed green tea, plus 25ml of ethanol for preservation, twice daily to the face for six weeks. No patients withdrew from the study. Student t-tests were used to determine significance. At baseline, the mean TLC was 24 and at the end of the six weeks the mean TLC was 10, a reduction of 58.33%, with statistically significant p value <0.0001 and a confidence interval (CI) of 8.58-19.42. The mean severity index (SI) also decreased after the six-week trial from 2.05 to 1.25, a 39.02% decrease with a statistically significant p value <0.0001 and a CI of 0.54-1.26. 3 of 20 (15%). 2 out of 20 patients complained of mild pruritus that developed at baseline and lasted three days. Clinical visits occurred every two weeks after baseline for eight weeks. A Wilcoxon signed-rank test was used to determine significance. The

mean revised Leeds score at baseline was 5.1; after eight weeks patients (10%) complained of stinging the first day of the study which resolved within 48 hours.

In Ji et al.'s study, 35 of the of 37 patients enrolled completed the eight-week study. The mean age of the patients was 22.1 with 17 males and 18 women. A side of each patient's face was randomly selected to receive either 1% or 5% EGCG solution. The opposite side of their face was then blindly given the control of 3% ethanol. With the 1% or 5% EGCG applied to the selected side of the face, the mean Leeds score significantly declined to 1.2 and 1.7, respectively by the end of the study. Noninflammatory lesions decreased from 53.8 to 15.6 and inflammatory lesions decreased from 10.0 to 1.1 with 1% EGCG which a is a 79% and 89% reduction respectively. The VAS scores were also significantly reduced from 10 to 3.5 with the 1% EGCG and from 10 to 4.9 in the 5% EGCG. In terms of numbers needed to harm (NNH) with every four persons treated with EGCG, one additional person will experience mild erythema or irritation.

In Lu et al. 80 women between the ages of 25-45 with moderate to severe acne were enrolled in the study and 64 completed the four-week intervention. Women who had systemic retinoid or hormone treatment in the past 3 months and/or women who had a systemic disease or dermatologic condition that could skew results were exempt from the study. Using computed randomization subjects, half were chosen to take one decaffeinated 500 mg green tea extract capsule, while the other half were given the placebo, pure microcrystalline cellulose capsules. Everyone was told to take a capsule 30 minutes after a meal daily for 4 weeks. BMI, hip and waist circumference, blood pressure, fasting glucose, and lipid profiles were also taken into account throughout the study and there were no significant differences between the control and experimental groups. Using paired t-tests, acne lesion counts on the nose, perioral area and chin significantly decreased with p values of 0.03, 0.04, and 0.03 respectively. Total inflammatory,

forehead, cheek, whole face and total non-inflammatory lesions did not significantly decrease all with p values >0.05 after treatment.

Table 2: Mean TLC and SI from baseline to 6 weeks[1]

	Baseline	After 6 weeks	% Reduction	P value
Mean TLC	24	10	58.33	<0.0001*
Mean SI	2.05	1.25	39.02	<0.0001*

*Signifies statistical significance ($p<0.05$)

Table 3: Mean Revised Leeds and VAS scores before and after treatment[4]

	Baseline	After 8 weeks
Mean Revised Leeds Score		
1% ECGC	5.2	1.2
5% EGCG	5.2	1.7
Mean VAS score		
1%	10	3.5
5%	10	4.9

Table 4: P values of acne lesion counts after 4 weeks of oral green tea extract[6]

Acne lesion counts	P values
Inflammatory	0.68
Forehead	0.76
Cheek	0.03*
Nose	0.04*
Perioral Area	0.03*
Chin	0.88
Whole face	0.41
Non-inflammatory	0.80

Table 3: Mean Revised Leeds and VAS scores before and after treatment[4]

	Baseline	After 8 weeks
Total	0.83	

*Signifies statistical significance ($p<0.05$)

Safety and Tolerability

In all three trials no major adverse side effects were reported and no subjects withdrew due to intolerability. In Elsaie et al. three out of twenty patients complained of mild pruritus lasting from the first day of application to day three, and two out of 20 patients complained of a mild stinging after first applying the lotion which lasted less than 48 hours. In Ji et al. NNH of four shows that one in every four patients will experience minimal irritation and stinging. In Lu et al. one subject developed mild constipation while two subjects complained of abdominal discomfort.

DISCUSSION

Based on the two double-blinded RCTs and one case study reviewed, green tea and the active substance within, EGCG, can significantly reduce lesion counts in males and females with acne vulgaris. However, these studies do have their limitations. In Lu et al. significance was not shown for total inflammatory and noninflammatory lesion counts and only showed significance for the nose, chin and perioral region. Hypotheses of why this study may not have had as much success include the way the green tea was administered, the population being studied, and the length of the trial. Starting off, this study was the only one in which the green tea byproduct was not used topically but administered orally through a capsule. Perhaps green tea is most potent when applied directly to lesions. Secondly, the Lu et al. study did not include any patients with mild acne vulgaris. This study also focused on adult women with acne and did not include

adolescents. Lastly, the Lu et al. study only lasted for four weeks, while the Elsaie and Ji studies lasted six and eight weeks respectively, a longer course.

These findings raise the question of whether or not green tea products are better treatments in mild to moderate acne, verses severe acne, or more effective in adolescents who have an increase in androgens and sebum verses adult women whose pathophysiology behind their acne may be more dependent on a different factor.[2] Additionally, it is unknown if six weeks of the oral green tea extract would have been as potent as six weeks of topical. None of these studies extended beyond two months so more controlled studies would be needed to provide a solidified answer as to the efficacy of the proposed treatment.

Additionally, EGCG was only isolated in one study, Ji et al., so it is unknown if the additional components of green tea used in the other two studies exacerbated or relieved acne as opposed to the isolated EGCG. It is also important to note that the exclusion criteria in Elsaie et al. and Ji et al. were not made clear and it is unknown if patients had previously been on hormonal therapy, isotretinoin, or retinoids and how recently, as well as if they have other dermatologic conditions. These factors could all play a role in the results of reductions in lesion counts.

CONCLUSION

Acne vulgaris is a condition suffered by millions and though treatments exist there is not one best option for all patients with equal efficacy. Effective treatments which focus on all factors in the development of acne, such as isotretinoin, do not come without extremely serious side effects.[4] After a systemic review of two double-blinded RCTs and one case study, it appears that the use of the anti-inflammatory polyphenol epigallocatechin-3-gallate in green tea could be a potential low-cost, natural alternative medicine for the treatment of acne. With minimal side

effects and shown improvement in acne, these green tea products can be an organic option for those who want to try a more benign treatment for their acne or to supplement their current routine. More research does need to be done, however. Future studies should focus on 1) the best formulation and/or administration of the green tea product; 2) which age group and which sex it is most effective for; and 3) the effectiveness of longer lengths of treatments.

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